## REMARKS

Further examination and reconsideration are respectfully requested in view of the foregoing amendments and following remarks.

**1. Status of the Claims**

Claims 1-30 stand pending. Claims 1-30 stand rejected. New claim 31 is added.

**2. Support for the Amendments**

The amendments are made to clarify the nature of the invention. Specifically, the addition of "temporal" to claims 1 and 16 is supported in the specification at page 22, lines 21-26, for example. New claim 31 incorporates a claim element from claim 17. The other amendments provide clarifying language suggested by the Examiner. The amendments thus do not add prohibited subject matter unsupported by the application as filed.

**3. Acceptance of the Formal Drawings**

Applicants note with appreciation the indication that the drawings submitted January 6, 2006, are deemed acceptable.

**4. Acknowledgement of Information Disclosure Statement**

Applicants note with appreciation the acknowledgement of the Information Disclosure Statement submitted August 25, 2008.

**5. Withdrawal of Restriction Requirement**

Applicants appreciate the withdrawal of the restriction requirement. No claims or species stand withdrawn.

**6. Withdrawal of the Notice of Non-Compliant Amendment**

Applicants note with appreciation the Notice of Non-Compliant Amendment mailed November 17, 2008, is withdrawn.

## 7. Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 4, 7-10, and 12-30 variously stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants appreciate the Examiner's suggestions for clearer language.

### Claim 4

Claim 4 is allegedly indefinite because of the phrase "gene is . . . barstar and protease inhibitors." The claim is amended as suggested by the Examiner, and the rejection accordingly may be withdrawn.

### Claims 7-8 and 24-25

Claims 7-8 and 24-25 are allegedly indefinite because of the phrase "characterized by." The phrase is replaced by "comprising," as suggested by the Examiner. The rejection may be withdrawn.

### Claims 9-10 and 26-27

Claims 9-10 and 26-27 allegedly equate genes with promoters. The amendments clarify the distinction between genes and promoters, according to the Examiner's suggestions. The rejection thus may be withdrawn.

### Claim 12

Claim 12 is allegedly indefinite for its use of abbreviations and for equating viruses with promoters. The amendment clarifies that MMV and FMV refer to constitutive promoters from mirabilis mosaic virus and figwort mosaic virus, respectively. The acronyms MMV and FMV are not spelled out in the specification, but the use of these acronyms for promoters from mirabilis mosaic virus and figwort mosaic virus, respectively, was well known in the relevant art. *See* Specification, page 29, line 43, through page 30, line 1; Day *et al.*, *Plant Mol. Biol.* 40: 771-82 (1999) (disclosing the mirabilis mosaic virus (MMV) promoter; U.S. Patent No. 5,378,619 (disclosing figwort mosaic virus (FMV) promoter).

### Claim 13

Claim 13 is allegedly indefinite for using improper Markush language and for not clearly stating that all the recited species contain the construct of claim 2 in their nuclear genome. The language of claim 13 is amended as recommended by the Examiner to clarify that the species are

recited in the alternative, and that all species contain the construct of claim 2 in their nuclear genome. The claim is now definite, and the rejection may be withdrawn.

**Claim 16**

Claim 16 is allegedly indefinite for failing to positively recite various claim elements and for using parentheses. The claim is amended to clarify the nature of the invention. In line 3 of part (a), a "wherein clause" is used in place of the Examiner's suggested language for greater clarity. Otherwise, the Examiner's suggestions are adopted to clarify the claim language. The claim is now definite, and the rejection accordingly may be withdrawn.

**Claim 17**

Claim 17 is allegedly indefinite for the use of the word "preferably." The term is deleted by amendment, and the rejection may be withdrawn. "*Brassica juncea*" is deleted from claim 17 and added to new claim 31. Claim 18 is amended to depend from new claim 31, so that "*Brassica juncea*" in claim 18 has a proper antecedent basis. Claim 17 is now definite, and the rejection thus may be withdrawn.

**7. Rejections under 35 U.S.C. § 103(a)**

**The Combination of Flasinski, Fabijanksi, and Shah**

Claims 1-2, 5-6, and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. 2006/0191038 ("Flasinski") in view of U.S. Patent No. 6,162,964 ("Fabijanski") and further in view of Shah *et al.*, *Proc. Nat'l Acad. Sci. USA* 79: 1022-1026 (1982) ("Shah").

Applicants traverse the rejection. The present claims are directed to a DNA construct and a method of using a DNA construct. The DNA construct contains two different coding sequences of a fertility restorer gene, both of which encode the same protein product, the first sequence being a naturally occurring wild type gene sequence and the second sequence being a modified sequence using degenerate codons. The wild type and modified gene sequences are under the control of different tissue specific promoters, which have overlapping temporal expression patterns in male reproductive tissues of the crop plant.

In one exemplary embodiment (*see, e.g.*, Specification, page 22, line 5, through page 23, line 11), the different promoters with overlapping temporal expression patterns are the A9 and TA29 promoters. In this embodiment, the A9 and TA29 promoters drive the expression of a *barstar* gene to restore male fertility. The data in Table 3 demonstrate that a construct comprising both promoters greatly increases the percent of restored plants, compared to the percentages obtainable using constructs with only one of the promoters.

The specification explains that this advantage is realized because the A9 and TA29 promoters have overlapping temporal expression profiles, ensuring effective inhibition of barnase:

> On using construct A [A9-bs(fm)::TA29-bs(wt)], the frequency of fertile plants registered a substantial increase to 89.8% indicating that barstar levels are significantly higher as compared to the earlier (control) constructs. In fertile plants derived using construct A, the presence of two independent transcriptional units for the barstar gene leads to the formation of more barstar mRNA and hence more barstar protein. Since the tapetum-specific promoters used to transcribe the barstar gene have overlapping expression profiles, accumulation of barstar protein in tapetal tissues begins earlier (from the A9 promoter) than barnase (which is under transcriptional control of the TA29 promoter) and continues during the entire period when barnase is expressed (from the TA29-barstar cassette). Extended expression of the barstar gene therefore builds up a reservoir of the inhibitor protein which ensures effective inhibition of barnase.

(page 23, lines 1-11) The claims reflect the advantage conferred by overlapping temporal expression patterns, where they recite that the construct comprises "different tissue-specific promoters having overlapping temporal expression patterns in male reproductive tissues of said crop plants." The specification discloses a number of promoters having the same advantageous properties as the A9 and TA29 promoters. *See, e.g.*, Specification, page 20, lines 1-14.

The primary reference, Flasinski, discloses constructs for expressing genes in transgenic plants. Flasinski discloses constructs comprising two separate promoters that function in plants, each of which is operably linked to a wild type gene sequence and a modified wild type sequence with degenerate codons. *See* Flasinski, ¶ 77. Flasinski discloses a long list of plant promoters, but fails to disclose a particular preference for any particular promoter. *See* Flasinski, ¶¶ 218-230. Even in this long list of promoters, Flasinski apparently fails to disclose any promoters specifically expressed in male reproductive tissues of crop plants, let alone such promoters that

have overlapping temporal expression patterns. The Office certainly provides no evidence that Flasinski recognized the advantages of using two such promoters in restoring male fertility.

Fabijanski does not remedy this deficiency of Flasinski. Fabijanski teaches the use of male sterility-inducing genes and male fertility-restoring genes, each under the control of male tissue-specific promoters. Fabijanski also teaches the use of marker genes, such as herbicide resistance genes, under the control of constitutive promoters, such as the CaMV 35S promoter. The Office alleges that the combination of Flasinski and Fabijanski would have suggested the use of a construct comprising two male tissue-specific promoters, each operably linked to a wild type gene sequence and a modified wild type sequence with degenerate codons, which could be used for restoring male fertility.

The Office provides no evidence, however, that Fabijanski teaches or suggests using two different male tissue-specific promoters with ***overlapping temporal expression patterns***. So Fabijanski, like Flasinski, does not recognize the advantages of using the claimed promoters, which substantially increase the percentage of male fertility-restored plants (*see, e.g.*, Specification, page 22, line 5, through page 23, line 11).

Finally, the Office cites Shah for the proposition that it would have been obvious to use an actin gene sequence as the male fertility-restoring gene sequence. Accepting the Office's allegation *arguendo*, the combined references still do not suggest the claim element of a gene construct comprising two different male tissue-specific promoters with overlapping temporal expression patterns.

*Prima facie* obviousness may be established only where the combination of references teaches or suggest each element of the claims. *See, e.g.*, *In re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). In the present case, however, the combined references do not teach at least the claim element of using different male tissue-specific promoters with overlapping temporal expression patterns. Without teaching this limitation, there can be no expectation of success. Accordingly, the Office fails to establish *prima facie* obviousness, and the rejection should be withdrawn.

**The Combination of Flasinski, Fabijanski, Shah, and Jagannath**

Claims 1-2, 5-6, and 9-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski further in view of Shah and further in view of Jagannath *et al.*, *Mol. Breeding* 8: 11-12 (2001).

Applicants traverse the rejection. The combined teachings of Flasinski, Fabijanski, and Shah are set forth above. The Office cites Jagannath for the proposition that it would have been obvious to use ***both*** the A9 and TA29 tapetum-specific promoters in the construct suggested by Flasinski, Fabijanski, and Shah. Jagannath suggests, however, using ***either*** the A9 or the TA29 promoter—but not both—in a construct to restore male fertility. Jagannath further provides evidence that the A9 and TA29 promoters are not "equivalent elements," as the Office alleges. *See* Office Action, p. 10, ¶1.

Jagannath teaches developing male sterile lines in *Brassica juncea.* Jagannath induces male sterility by expressing *barnase* under control of the A9 promoter or the TA29 promoter. *See* Jagannath, FIG. 1. Jagannath finds that male sterility can be induced with a higher frequency when a Spacer DNA is inserted between the *barnase* gene and the *bar* gene. *See, e.g.*, Jagannath, Abstract; p. 18, last ¶. Jagannath concludes that the TA29-*barnase* construct efficiently induces male sterility, using the Spacer DNA. Jagannath also concludes, however, that the A9 promoter was inefficient in this application (p. 18, 2d col.):

> The above results indicate that use of a 3 kb Spacer fragment with the A9 promoter does not confer sufficient protection against deregulated expression of the *barnase* gene while use of a 5 kb Spacer fragment adequately protects [the] tissue-specific expression of the TA29 promoter.

So while Jagannath arguably suggests using the TA29 promoter in a construct (which further comprises a Spacer DNA) to induce male sterility, Jagannath teaches that the A9 promoter is not equivalent to the TA29 promoter for this purpose. Jagannath instead teaches away from using the A9 promoter. Further, Jagannath teaches only the creation of male sterile lines, not restoration of male fertility.

For the reasons above, Jagannath, like Flasinski and Fajijanski, does not suggest using a construct comprising two different tissue-specific promoters, e.g., the A9 and TA29 promoters, having overlapping temporal expression patterns in male reproductive tissues of crop plants. To

the contrary, Jagannath suggests using either the A9 or the TA29 promoter. Jagannath further concludes that the A9 promoter is unsuitable for its intended use in the construct. Even if, for the sake of argument, the artisan of ordinary skill would have used the TA29 promoter, the artisan would not have used a construct comprising ***both*** the A9 and TA29 promoters, as recited. *See, e.g. W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550 (Fed. Cir. 1983) (holding that all relevant teachings of cited references must be considered in determining what they fairly teach to one having ordinary skill in art, including those aspects of the reference that teach away from the claimed invention). Accordingly, the Office has not made a *prima facie* case of obviousness, and the rejection should be withdrawn.

**The Combination of Flasinski, Fabijanski, Jofuku and Stevenson**

Claims 1-6 and 11-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski, further in view of Jofuku *et al.*, *Plant Cell* 1: 1079-93 (1989) ("Jofuku") and Stevenson *et al.*, *Nucl. Acids Res.* 14: 8307-30 (1986) ("Stevenson").

Applicants traverse the rejection. The Office applies the combined references to suggest modifying the construct allegedly suggested by the combination of Flasinski and Fabijanski. Specifically, the Office combines the teachings of Jofuku and Stevenson to suggest a construct comprising a male sterility gene encoding a protease, such as trypsin, and a male fertility restorer gene encoding a protease inhibitor, such as trypsin inhibitor. Even assuming for the sake of argument that the combined teachings would have suggested the use of gene sequences encoding trypsin and trypsin inhibitor, the combined teachings do not teach or suggest the claim element of using two different male tissue-specific promoters with overlapping temporal expression patterns. Accordingly, the Office fails to establish *prima facie* obviousness, and the rejection should be withdrawn.

**The Combination of Flasinski, Fabijanski, Jofuku, Stevenson, and Jagannath**

Claims 1-6 and 9-15 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski and further in view of Jofuku, Stevenson, and Jagannath.

Applicants traverse the rejection. The teachings and deficiencies of the cited references are set forth above. For the reasons set forth above, the combined references neither teach nor

suggest the claim element of a construct comprising different tissue specific promoters having overlapping temporal expression patterns in male reproductive tissues of crop plants. *Prima facie* obviousness is not established, and the rejection thus should be withdrawn.

**The Combination of Flasinski, Fabijanski, Williams, and Michiels**

Claims 1-7, 9, 11-24, 26, and 28-30 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski and further in view of U.S. Patent No. 5,750,867 ("Williams") and U.S. Patent No. 6,372,960 ("Michiels").

Applicants traverse the rejection. The teachings of Flasinski and Fabijanski and their deficiencies are set forth above. Williams teaches a construct comprising a fertility restorer gene sequence operably linked to a promoter, such as the TA29 promoter. The Office particularly points to the teaching in Williams of a *barstar* sequence essentially identical to the recited sequence of SEQ ID NO: 1. Michiels further teaches a codon-optimized variant of a *barstar* gene. The Office alleges it would have been obvious to use both *barstar* gene sequences in the construct suggested by the combination of Flasinski and Fabijanski. Even if this were true *arguendo*, the Office fails to provide a teaching or suggestion in Williams or Michiels to use a construct comprising different male tissue-specific promoters with overlapping temporal expression patterns. Neither Williams nor Michiels thus correct the deficiencies of Flasinski and Fabijanski. *Prima facie* obviousness is not established, and the rejection thus should be withdrawn.

**The Combination of Flasinski, Fabijanski, Williams, Michiels, and Jagannath**

Claims 1-7, 9-24, and 26-30 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Flasinski in view of Fabijanski and further in view of Williams , Michiels, and Jagannath.

Applicants traverse the rejection. The teachings and deficiencies of the cited references are set forth above. For the reasons set forth above, the combined references neither teach nor suggest the claim element of a construct comprising different tissue specific promoters having overlapping temporal expression patterns in male reproductive tissues of crop plants. *Prima facie* obviousness is not established, and the rejection thus should be withdrawn.

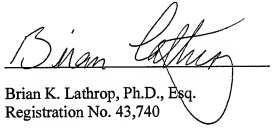
## CONCLUSION

The claims are believed ready for allowance. If there are any other fees due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

**DRINKER, BIDDLE & REATH LLP**

Dated: June 29, 2009

By: 

Brian K. Lathrop, Ph.D., Esq.
Registration No. 43,740

**CUSTOMER NO. 55694**
**DRINKER, BIDDLE & REATH LLP**
1500 K Street, N.W., Suite 1100
Washington, D.C. 20005-1209
Tel: (202) 842-8800
Fax: (202) 204-0289